

REMARKS**I. Applicants' Invention and Preliminary Comments.**

Applicants' invention relates to the discovery that 1) replacing at least 5% of an individual's daily carbohydrate intake with resistant starch, and 2) at least 10% of the individual's saturated fat intake with unsaturated fat provides numerous improvements to carbohydrate and lipid metabolism including: a) enhancing carbohydrate and fat metabolism, b) reducing plasma leptin concentrations, c) increasing satiety, d) lowering the risk of obesity, e) lowering the risk of non-insulin dependent diabetes mellitus, f) lowering post-prandial glucose and/or insulin levels, and g) helping control an individual's body mass.

To examine in detail the metabolic effects of diet on the regulation of carbohydrate and fat metabolism, Applicants investigated the effect of four diets on plasma glucose, plasma insulin, plasma leptin and C-fos brain activity following a 16 week dietary protocol. (See Figures 4-6 and the accompanying Declaration Under 37 C.F.R. 1.132 of Ian L. Brown). The four diets comprised: 1) saturated fat/amylopectin; 2) saturated fat/amylose; 3) unsaturated fat (N-3)/amylopectin; and 4) unsaturated fat (N-3)/amylose. Results showed that for plasma glucose concentrations, in response to a 2-hour intravenous glucose challenge, the saturated fat/amylopectin diet is significantly different from the unsaturated fat (N-3)/amylopectin diet, while the unsaturated fat(N-3)/amylose diet is significantly different from the unsaturated fat (N-3)/amylopectin. (See Figure 4). With regard to fasting leptin concentrations, there were significant differences between the starch groups. (See Figure 5). Specifically, it was shown that consumption of a diet high in resistant starch and unsaturated fats or lipids leads to reduced post-prandial plasma glucose concentrations after meal-intake, as well as lower plasma insulin levels and a reduction in plasma leptin concentrations.

Further results showed that transcription of c-fos is modulated significantly in the dorsomedial hypothalamic nucleus (DHM), arcuate hypothalamic nucleus (ARC), lateral hypothalamus (LH), paraventricular hypothalamic nucleus (PVN) and ventromedial hypothalamic nucleus (VMH) in response to diet. C-fos transcription is a good indicator of neuronal activity. The observations made are important since these regions of the brain are known to play a role in regulation of energy and balance and satiety. The data from neuronal

(c-fos) activity presents evidence that diets high in unsaturated fats and resistant starch have decreased activation of the hunger center (LHA) whereas diets high in saturated fat and low in resistance starch have the opposite effect. The results are consistent with the changes in satiety and plasma leptin concentrations. The unexpected finding that consumption of a diet high in resistant starch and unsaturated fats results has desirable effects on plasma glucose, plasma insulin, plasma leptin and C-fos brain activity provides valuable information for the regulation of carbohydrate and fat metabolism in an individual.

The specification has been amended in order to correct an obvious typographical error with respect to the identification of the Table in which results are reported. A review of the Figures 1-6 and Table 2 shows that the results reported in Table 2 corresponds to the results of Figures 1-3 rather than those of Figures 4-6. The error is an obvious one and no new matter is introduced by the forgoing amendment.

II. Outstanding Rejections

Claims 1-10, 26-33 and 35 stand rejected under 35 U.S.C. §103(a) over Noakes et al., *The American Journal of Clinical Nutrition*, Vol. 64, pages 944-951 (1996); in view of Hitz et al. *U.S. Patent Reissue No. RE 37,317 E*.

III. Patentability Arguments

A. The Rejection Under 35 U.S.C. §103(a) over Noakes et al. and Hitz et al. should be withdrawn.

The obviousness rejection over Noakes et al. and Hitz et al. should be withdrawn because Noakes et al. teach that replacing carbohydrates with resistant starch in a diet: 1) showed no benefit in insulin sensitivity or plasma lipid responses, 2) caused dyslipidemia to worsen, and 3) accentuated the risk of coronary artery disease. This teaches away from Applicants' discovery that replacing carbohydrates and lowering fats in a diet has the benefits of a) reducing plasma leptin concentrations, b) lowering the incidence or risk of non-insulin dependent diabetes mellitus, and c) reducing post-prandial glucose and/or insulin levels.

Specifically, Noakes et al. teach that replacing as much as 25% of an overweight hyperglyceridemic subject's daily carbohydrate intake with resistant starch does not have a

positive metabolic effect on plasma lipids and that replacing as much as 33% had only a small reduction in plasma insulin concentrations. (See page 8, third paragraph). In addition, Noakes et al. suggest that such replacements in combination with changes in fat intake can cause dyslipidemia to worsen. Specifically, Noakes et al. teach that:

"other studies that have made similar dietary changes in carbohydrate and fat (8,9) or fibre separately have not shown any benefit in insulin sensitivity or plasma lipid responses and, in fact, dyslipidemia has been shown to worsen." (See Abstract, lines 15-18).

In addition, Noakes et al. cites Liu et al, *Metabolism*, 32(8):750-3, (1983) (reference 8 cited by Noakes et al., attached hereto as Exhibit A), which further discloses that:

"low-fat, high-carbohydrate diets accentuate the metabolic risk factors for coronary artery disease that are already present in patients endogenous hypertriglyceridemia."

Thus, Noakes et al. teach away from replacing low concentrations of carbohydrates in a diet with resistant starch and making changes in fat intake for the purposes of reducing plasma lipids and postprandial insulin concentrations. Moreover, Noakes et al. do not disclose or suggest that at least 10% of the saturated fat should be replaced with unsaturated fat or that such a replacement would achieve the health benefits recited in the claims of the present invention.

While Hitz et al. is directed to the effects of diets high in mono-unsaturated fat and low in saturated fat it fails to make up for the deficiencies of Noakes et al. with respect to the effect of relatively low levels of resistant starches. In fact Hitz et al. make no reference to benefits of modifying carbohydrate intake at all.

Accordingly, the cited references fail to teach that replacing as little as 5% of an individual's daily carbohydrate with resistant starch in combination with replacing at least 10% of an individual's saturated fat intake with unsaturated fat would be successful in achieving the health benefits recited in the claims of the present invention. Accordingly, the rejection on the basis of Noakes et al. and Hitz et al. should be withdrawn and each of claims 1-10, 26-33 and 35 should be allowed.

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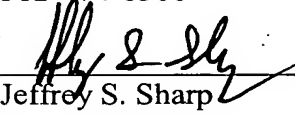
CONCLUSION

For all of the foregoing reasons, the rejection should now be withdrawn and an early notice of all pending claims is respectfully solicited. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, he is invited to contact the undersigned attorney at the number indicated below.

Respectfully submitted,

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